REMARKS

Upon entry of the foregoing amendments to the specification, the title has been amended. Also, the specification has been amended as shown above to remove URLs from the specification. No new matter has been added by the amendments to the title or the specification.

The claims have been amended as set forth above. Upon entry of the above-described amendments and new claims, Claims 27-29, 32-34 and 38-51 are pending. Claims 22-26, 30-31 and 35-37 have been cancelled without prejudice toward future prosecution. Claims 27-29 and 32-33 have been amended to remove reference to the Figures. Claim 27 has been amended to remove reference to the extracellular domain. Claim 38 has been amended to depend from Claim 27, rather than cancelled Claim 22. Claim 40 has been amended to recite "isolated" host cell.

New Claims 42-51 are submitted. The new claims are supported by the original claims and specification as filed. New Claims 42-43 and 48 include the limitation that the claimed nucleic acid encodes a polypeptide that has the ability to induce mesangial cell proliferation or to induce fetal hemoglobin. Support for this limitation is found in Examples 40 and 41 on page 168, describing a mesangial cell proliferation assay (Assay #92) and fetal hemoglobin induction assay (Assay #107). No new matter is added by the amendments and the claims are fully supported by the specification as originally filed.

Applicants respond below to the specific rejections raised by the PTO in the Office Action mailed March 23, 2005. For the reasons set forth below, Applicants respectfully traverse.

Correction of Inventorship under 37 CFR §1.48(b)

Applicants request that several inventors be deleted, as these inventors' inventions are no longer being claimed in the present application as a result of prosecution. The fee as set forth in § 1.17(i) is submitted herewith.

Information Disclosure Statement

The Examiner states that the previously-filed information disclosure statements have been considered, but do not give sufficient identifying information to determine if the sequences constitute prior art.

Applicants submit herewith an Information Disclosure Statement that includes more detailed information regarding the BLAST results, including the publication date of the relevant sequences.

Specification

The Examiner states a new title is required that is more clearly indicative of the invention to which the claims are directed. The title has been amended to recite "NUCLEIC ACIDS ENCODING POLYPEPTIDES THAT INDUCE CELL PROLIFERATION OR INDUCE FETAL HEMOGLOBIN."

Also, the Examiner states that the specification should be reviewed for the recitation of improper hyperlinks, and that all such recitations should be deleted or amended. Applicants have amended the specification to address the Examiner's concern. In particular, Applicants have replaced the hyperlinks with text that describes the location of the websites. The amended text no longer constitutes browser executable code.

Rejections under 35 U.S.C. §112, first paragraph – Enablement

The Examiner has rejected Claims 22-27, 30-31 and 35-41 as lacking enablement. The Examiner acknowledges that the encoded PRO4408 peptides have utility under § 101 based upon the ability of the peptides to induce fetal hemoglobin. The Examiner argues that the "claims encompass an unreasonable number of inoperative polynucleotides, which the skilled artisan would not know how to use." Furthermore, the Examiner argues that the "specification does not provide guidance for using polypeptides related to (i.e., 80%-99% identity) but not identical to SEQ ID NO:61 which do not have the single specific disclosed activity shown for nucleic acids encoding PRO4408." Thus, the Examiner asserts that the claims are broad because they do not require the claimed nucleic acid to encode a polypeptide identical to the disclosed sequence and because the claims have no functional limitation.

As set forth above, Claims 22-26, 30-31 and 35-37 have been cancelled, and thus will not be discussed further in connection with this rejection. The pending independent claims, Claims 27, 42 and 48 are fully enabled at least for the reasons set forth below.

Applicants respectfully submit that independent Claim 27 is fully enabled because Applicants have taught how to make and use the claimed sequences. For example, Applicants

have provided the complete sequence of the sequence of SEQ ID NO:60, the sequence of the cDNA deposited under ATCC accession number 203971, as well as the sequence that encodes the polypeptide of SEQ ID NO:61. Also, a function has been described for the encoded polypeptide sequence based upon Example 40 (Assay #107) or Example 41 (Assay #92) such that one of skill in the art would know how to use the encoded polypeptide. The specification further provides ample teaching regarding uses for the nucleic acids as claimed in Claim 27. For example, see page 119, line 5 to page 123, line 7. Thus, Claim 27 is fully enabled.

New independent Claims 42 and 48 recite the functional limitation "wherein said isolated nucleic acid encodes a polypeptide that has the ability to induce mesangial cell proliferation or to induce fetal hemoglobin." In view of this, the specification teaches how to make and use the claimed subject matter. Specifically, the specification describes how to make the claimed variant nucleic acids and the encoded polypeptides (for example, see page 109, line 7 to page 111, line 16). Furthermore, one of skill in the art would know how to follow Example 40 or Example 41 to assay for the claimed function in the encoded variant polypeptides. Also, as mentioned above, the specification discloses uses for the nucleic acids. Based upon that teaching, one skilled in the art would know how to make and use the full scope of the claimed subject matter.

Therefore, Applicants request that the Examiner reconsider and withdraw the enablement rejection under 35 U.S.C. § 112, first paragraph.

Rejections under 35 U.S.C. §112, first paragraph – Deposit Requirements

Claims 22-27 and 34-41 are rejected as not complying with the enablement requirement, since the deposit requirements were not met. The Examiner requests a statement that the deposit "will be maintained for a term of at least 30 years and at least five (5) years after the most recent request for the furnishing of sample of the deposit was received by the depository."

Respectfully, this requirement has already been met. As noted by the Examiner, the deposit was made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). However, the Examiner argues that this statement only provides partial compliance with the deposit requirement and requests the above statement. Applicants assert that they have fully complied with the requirement by stating that the deposit was made under the provisions of the Budapest Treaty because deposit under the Treaty universally requires

that the depositor agree not to withdraw the deposited material for a period of five years after the most recent request for a sample, and in any case at least 30 years after deposit (per Rule 9.1).

Nonetheless, enclosed is a Declaration under 37 C.F.R. §1.808 that states that the deposit will be maintained for a term of at least 30 years and at least five (5) years after the most recent request for the furnishing of sample of the deposit was received by the depository.

Rejections under 35 U.S.C. §112, first paragraph – Written Description

The Examiner asserts that Claims 22-27, 30-31 and 33-34 contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner argues that "[t]he claims do not require that the claimed polynucleotide encode a particular protein, nor that any protein encoded thereby possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature."

The Legal Standard for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112 , first paragraph is whether the disclosure "reasonably conveys to artisan that the inventor had possession at that time of the later claimed subject matter." *In re Kaslow*, 707 F.2d 1366, 1375, 2121 USPQ 1089, 1096 (Fed. Cir. 1983); *see also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. *See e.g., Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 USPQ2d at 1116 (Fed. Cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. *Union Oil v. Atlantic Richfield Co.*, 208 F.3d 989, 996 (Fed. Cir. 2000).

As set forth above, Claims 22-26, 30-31 and 35-37 have been cancelled, and thus will not be discussed further in connection with this rejection. The pending independent claims, Claims 27, 42 and 48 are described at least for the reasons set forth below.

Applicants respectfully submit that independent Claim 27 is fully described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, possessed the claimed subject matter. For example, Applicants have disclosed in the specification the complete sequence of the sequence of SEQ ID NO:60, the sequence of the cDNA deposited under ATCC accession number 203971, as well as the sequence that encodes the polypeptide of SEQ ID NO:61. No additional information is required, and thus, Claim 27 is fully described.

New independent Claims 42 and 48 recite that the claimed variant nucleic acids encode a polypeptide "that has the ability to induce mesangial cell proliferation or to induce fetal hemoglobin." Also, the claims include percent identity limitations, 98% and 99%, respectively. Accordingly, Applicants maintain that the claims recite sufficient distinguishing characteristics for the claimed genus of nucleic acids. Based on the detailed description of the cloning and expression of variant sequences encoding PRO4408 in the specification, the description of the assays in Examples 40 and 41, the actual reduction to practice of sequences SEQ ID NOs: 60 and 61, and the functional recitation in the instant claims, Applicants submit that one of skill in the art would know that Applicants possessed the invention as claimed in the instant claims.

Hence, Applicants respectfully request that the PTO reconsider and withdraw the written description rejection under 35 U.S.C. §112.

Rejections under 35 U.S.C. §112, second paragraph

The Examiner has rejected Claims 22-27, 30-31 and 34-41 under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner states that "[c]laims that recite 'the extracellular domain' of the protein are indefinite as no extracellular domain has been described." Further according to the Examiner, if the polypeptide possesses an extracellular domain, the recitation of "the extracellular domain … lacking its associated signal sequence" is indefinite because a signal sequence is generally not considered to be part of an extracellular domain.

As set forth above, Applicants have removed reference to the extracellular domain from the claims. Therefore, this rejection is moot and its withdrawal is requested.

The Examiner also argues that Claim 35 reciting "hybridizes to" and Claim 36 reciting "stringent" conditions are indefinite because what will hybridize to a given sequence is dependent upon the conditions of hybridization and washing.

Again, Claims 35 and 36 have been cancelled. Therefore, this rejection is moot and not further discussed herein.

Rejection under 35 U.S.C. §102 – Anticipation

U.S. Patent Nos. 6,063,767 and 5,888,742:

The Examiner has rejected Claims 22-26 and 35-41 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent Nos. 6,063,767 and 5,888,742. The '767 patent is a divisional of the '742 patent. The Examiner argues that SEQ ID NO:4 from the cited patents is 96.5% identical to the instant SEQ ID NO:60. The Examiner further argues that SEQ ID NO:4 of the cited references discloses a sequence that is 99.4% identical to the full-length coding region of SEQ ID NO:60. The Examiner argues that the sequences of the cited patents will hybridize to SEQ ID NO:60. Respectfully, Applicants argue that the '767 and '742 patents do not anticipate the pending independent claims or any dependents therefrom.

The rejection of Claims 22-26 and 35-37 will not be addressed further as those claims have been cancelled. Claim 38 now depends from Claim 27 which was not rejected as being anticipated.

New Claim 42 is not anticipated by the '767 patent or the '742 patent because the nucleic acid sequences disclosed in the cited patents do not disclose "an isolated nucleic acid encoding a polypeptide having at least 98% amino acid sequence identity to the polypeptide of SEQ ID NO:61 or to the polypeptide of SEQ ID NO:61 lacking its associated signal peptide." The polypeptide disclosed in the cited patents, SEQ ID NO:3, which is encoded by SEQ ID NO:4, has at best only 97.8% identity to the polypeptide of SEQ ID NO:61 with or without its signal peptide (218/223 x 100 = 97.8%). Therefore, SEQ ID NO:4 from the cited patents does not encode a polypeptide with at least 98% identity to the instant polypeptide of SEQ ID NO:61. Thus, Claim 42 and the claims depending therefrom are not anticipated by the cited patents.

New Claim 48 also is not anticipated because, as acknowledged by the Examiner, the cited patents do not disclose an "isolated nucleic acid having at least 99% nucleic acid sequence identity to the nucleic acid sequence of SEQ ID NO:60." The nucleic acid of SEQ ID NO:4 of

the cited patents has less than 99% identity to the instant sequence of SEQ ID NO:60. Therefore, Claim 48 is not anticipated by the cited patents.

Locus G27363:

The Examiner also rejected Claims 35-37 under 35 U.S.C. §102(b) as being anticipated by locus G27363, published on June 28, 1996. This rejection is moot in view of the cancellation of Claims 35-37.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §102 because none of the cited references teaches each and every element of the claims.

Conclusion

The present application is believed to be in condition for allowance, and an early action to that effect is respectfully solicited. Applicants invite the Examiner to call the undersigned if any issues may be resolved through a telephonic conversation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 17, 2005

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